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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/897,898	07/05/2001	Harm M. Deckers	034547-0104	3117

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/897,898	DECKERS ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/31/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,15,18 and 29-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-15, 18 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a CIP of 09/448,755, now abandoned.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2007 has been entered.

Claims 14-15, 18 and 29-31 are pending and are under consideration.

Claim for Domestic Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent

application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/448,755, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. There is lack of enablement/description of a method of preparing an emulsion formulation comprising thioredoxins or thioredoxins reductase fused to an oil body protein or the central domain of an oleosin. Accordingly, claims 14-15, 18 and 29-31 are not entitled to the benefit of the prior applications.

When applicant files a continuation-in-part whose claims are not supported by the parent application, the effective filing date is the filing date of the child CIP. Any prior art disclosing the invention or an obvious variant thereof having a critical reference date more than 1 year prior to the filing date of the child will bar the issuance of a patent under **35 U.S.C. 102(b)**. *Paperless Accounting v. Bay Area Rapid Transit System,* 804 F.2d 659, 665, 231 USPQ 649, 653 (Fed. Cir. 1986) (MPEP 2133.01). Therefore, the effective filing date, for art purposes, is the filing date of the instant application, July 5, 2001.

Response to Arguments

Applicant's arguments filed October 31, 2007 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-15, 18 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moloney et al., Wieles et al., Rooijen et al. and Murphy et al.

Claims 14-15, 18 and 29-31 are drawn to a method of making an emulsion by transforming a plant cell, such as a rapeseed cell, with a chimeric polynucleotide

comprising a polynucleotide that regulates transcription in a cell linked to a polynucleotide encoding a fusion protein comprising at least the central domain of an oleosin and a thioredoxin or thioredoxin reductase which is further linked to a polynucleotide that terminates transcription in the plant cell, wherein oil bodies comprising the fusion protein is isolated and washed such that substantially intact oil bodies are obtained, which is then formulated into an emulsion. Claim 29 limits claim 14 in that the thioredoxin or thioredoxin reductase of the emulsion reduces a target.

Moloney et al. (WO 96/21029 - form PTO-1449) discloses method of producing a fusion protein by introducing into a plant cell, such as a rape seed host cell (page 26 and pages 36-37), a chimeric polynucleotide comprising a polynucleotide that regulates transcription in a cell linked to a polynucleotide encoding a fusion protein comprising a portion of an oleosin obtained from plant and a heterologous protein of interest which is further linked to a polynucleotide capable of terminating transcription in a plant cell, (pages 2-3). The oleosin used by Moloney et al. comprises at least the central domain (page 16, line 27). The method of Moloney et al. comprises growing said transformed plant host cell under conditions permitting expression of said fusion polypeptide, isolating oil bodies comprising said fusion polypeptide and washing said oil bodies comprised of intact oil bodies via centrifugation (pages 2-3 and 10-11). Centrifugation is given as an example of "washing oil bodies", page 12. Also, since Moloney et al. also teaches that the enzyme of the fusion protein retains its enzymatic properties (page 21) indicating the heterologous protein is intact, Examiner takes the position that the "washed oil body preparation" comprising the fusion protein of Moloney et al. is

"substantially intact". Moloney et al. provides several advantages in producing a heterologous protein in plant cells by expressing a fusion protein comprising the protein of interest and an oleosin, such as efficient large scale production of the protein (page 2, lines 1-9).

The difference between the reference of et al. and the instant invention is that the reference of Moloney et al. does not teach a method of emulsifying the washed oil bodies comprising the fusion protein, wherein the heterologous protein is a thioredoxin or a thioredoxin reductase.

Polynucleotides encoding many thioredoxin and thioredoxin reductases are known in the art see NiceZyme: EC 1.8.1.9 – cited previously on form PTO-892). Wieles et al. (cited previously on form PTO-892) discloses a polynucleotide encoding a thioredoxin and thioredoxin reductase and production of thioredoxin and thioredoxin reductase expressed in bacteria (abstract and pages 921-922). Wieles et al. also discloses that thioredoxin and thioredoxin reductase are involved in redox regulation and catalytic mechanism (abstract and page 921). Wielses et al. does not disclose expression and production of thioredoxin and thioredoxin reductase in plant cells or rapeseed cells.

Rooijen et al. (Biotechnology (N Y). 1995 Jan;13(1):72-7 - form PTO-1449) discloses a method of production and isolation of heterologous proteins in plant cells, such as rapeseed cells, by fusing a oleosin to the heterologous protein, wherein the oleosin facilities separation of the heterologous protein from other cellular proteins

(page 72 and abstract). Rooijen et al. discloses that said oleosin- heterologous protein fusion protein is enzymatically active and resides on the oil bodies and may be used directly in heterogeneous catalysis (abstract and Figure 5 on page 76). Rooijen et al. also discloses that after a round of catalysis the fusion protein may be recovered and reused several times without loss of activity and that production of these fusion proteins is extremely inexpensive, offering a novel route to the manufacture of recombinant proteins (abstract). Rooijen et al. also discloses that oil-bodies remain intact after aqueous extraction (or washing) (page 72). With the teachings of Rooijen et al. at hand, one having ordinary skill in the art would have recognized the advantage of producing thioredoxin and thioredoxin reductase using the method of Moloney et al. as opposed to its production in bacterial cells.

Murphy et al. (INFORM. Vol. 4. no. 8 (August 1993) – form PTO-1449) discloses that oleosins have a central hydrophobic domain (page 925, central column), which permits the oleosin to be embedded in oil bodies. With this teaching at hand, one having ordinary skill in the art would have recognized to use an oleosin comprising its central hydrophobic domain or full length oleosin. Murphy et al. also discloses that oleosins act as emulsifying agents and/or as emulsion-stabilizing agents (page 931).

Therefore, combining the teachings of Moloney et al., Wieles et al., Rooijen et al. and Murphy et al., it would have been obvious to one having ordinary skill in the art to modify the method of Moloney et al. by making a chimeric construct comprising a fusion protein wherein the heterologous protein is the thioredoxin or thioredoxin reductase of Wieles et al. and the portion of an oleosin is a central domain of an oleosin, express the

chimeric construct in a rapeseed cell and to formulate the fusion protein into an emulsion. One of ordinary skill in the art would have been motivated to use thioredoxin or thioredoxin reductase as the heterologous protein in the fusion protein of Moloney et al. in order to inexpensively produce thioredoxin and thioredoxin reductase in plant cells, wherein the fusion protein can be re-used several times in catalysis. One of ordinary skill in the art would have been motivated to use oleosins comprising its central domain because Murphy et al. teaches that the central domain of oleosins are hydrophobic, which allows the oleosin to be embedded into the oil body. One of ordinary skill in the art would have been motivated to formulate the fusion protein into an emulsion to increase stability of the fusion protein for its re-use in catalysis. One of ordinary skill in the art would have had a reasonable expectation of success of making a fusion protein and isolating the fusion protein since Moloney et al. disclose a method of making a polynucleotide encoding a fusion proteins comprising oleosins and heterologous protein and Rooijen et al. discloses production of said fusion protein in a rapeseed cell and isolation of the fusion protein. One of ordinary skill in the art would have had a reasonable expectation of success in making an emulsion comprising said fusion protein since Murphy et al. teaches that oleosins are emulsifying agents.

Therefore, the above references render claims 14-15, 18 and 29-31 *prima facie* obvious to one of ordinary skill in the art.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the combined teachings of the cited reference would not have led to the clamed method because all of the claim recitations are not found in the asserted combination and points to Moloney et al. as failing to teach "emulsifying the fusion protein comprising a thioredoxins or thioredoxin reductase" and "formulating into an emulsion a washed oil body preparation that comprises a 'recombinant fusion polypeptide'". Examiner respectfully disagrees. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The reference of Murphy et al. (INFORM. Vol. 4. no. 8 (August 1993) – form PTO-1449) is relied upon for its teaching that oleosins act as emulsifying agents and/or as emulsion-stabilizing agents (page 931), wherein the central hydrophobic domain permits the oleosin to be embedded in oil bodies(page 925, central column). With this teaching at hand, one of ordinary skill in the art would have been motivated to formulate the fusion protein into an emulsion to increase stability of the fusion protein for its re-use in catalysis.

Applicants argue that Murphy et al. neither teaches nor suggests formulating into an emulsion a washed oil body preparation that comprises a recombinant fusion polypeptide. Examiner respectfully disagrees. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800

F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). A fusion polypeptide comprising oleosin and a thioredoxins is made obvious by the combined teachings of of Moloney et al., Wieles et al. and Rooijen et al. As discussed above, the reference of Murphy et al. is relied upon for its teaching that oleosins act as emulsifying agents and/or as emulsion-stabilizing agents (page 931), wherein the central hydrophobic permits the oleosin to be embedded in oil bodies domain (page 925, central column). Therefore, it would have been obvious to one having ordinary skill in the art to modify the method of Moloney et al. by making a chimeric construct comprising a fusion protein wherein the heterologous protein is the thioredoxin or thioredoxin reductase of Wieles et al. and the portion of an oleosin is a central domain of an oleosin, express the chimeric construct in a rapeseed cell and to formulate the fusion protein into an emulsion. One of ordinary skill in the art would have been motivated to formulate the fusion protein into an emulsion to increase stability of the fusion protein for its re-use in catalysis.

Applicants argue that combining Moloney et al. with Wieles et al. and/or Rooijen et al. does not cure the deficiencies in Moloney et al., formulating an emulsion. Examiner respectfully disagrees. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The rejection is based on the combined teachings of Moloney et al. with Wieles et al., Rooijen et al. and Murphy et al. The reference of Murphy et al. (INFORM. Vol. 4. no. 8 (August 1993) – form PTO-1449) is relied upon for

its teaching of that oleosins act as emulsifying agents and/or as emulsion-stabilizing agents (page 931), wherein the central hydrophobic domain (page 925, central column), permits the oleosin to be embedded in oil bodies. With this teaching at hand, one of ordinary skill in the art would have been motivated to formulate the fusion protein into an emulsion to increase stability of the fusion protein for its re-use in catalysis.

Applicants argue that the rationale for combining the cited references would fall short of the claimed invention because the references do not suggests a method for preparing an emulsion by (1) obtaining intact oil bodies, (2) washing the intact oil bodies and (3) formulating the washed oil body preparation into an emulsion. Examiner respectfully disagrees. The instant rejection is not an anticipatory rejection, but an obviousness rejection. "Obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so" (MPEP 2143.01). (1)-(2) Moloney et al. teaches isolating oil bodies comprising a fusion protein and washing said oil bodies comprised of intact oil bodies via centrifugation (pages 2-3 and 10-11). Centrifugation is given as an example of "washing oil bodies", page 12. Also, since Moloney et al. also teaches that the enzyme of the fusion protein retains its enzymatic properties (page 21) indicating the heterologous protein is intact, Examiner takes the position that the "washed oil body preparation" comprising the fusion protein of Moloney et al. is "substantially intact". (3) As discussed above, Murphy et al. teaches that oleosins act as emulsifying agents and/or as emulsion-stabilizing agents (page 931), wherein the central hydrophobic domain (page 925, central column), permits the oleosin to be

embedded in oil bodies. With this teaching at hand, one of ordinary skill in the art would have been motivated to formulate the fusion protein into an emulsion in order to increase stability of the fusion protein for its re-use in catalysis.

Hence the rejection is maintained.

Claims 14-15, 18 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moloney et al., Wieles et al., and Deckers et al.

Claims 14-15, 18 and 29-31 are drawn to a method of making an emulsion by transforming a plant cell, such as a rapeseed cell, with a chimeric polynucleotide comprising a polynucleotide that regulates transcription in a cell linked to a polynucleotide encoding a fusion protein comprising at least the central domain of an oleosin and a thioredoxin or thioredoxin reductase which is further linked to a polynucleotide that terminates transcription in the plant cell, wherein oil bodies comprising the fusion protein is isolated and washed such that substantially intact oil bodies are obtained, which is then formulated into an emulsion. Claim 29 limits claim 14 in that the thioredoxin or thioredoxin reductase of the emulsion reduces a target.

Moloney et al. (WO 96/21029 - form PTO-1449) discloses method of producing a fusion protein by introducing into a plant cell, such as a rape seed host cell (page 26 and pages 36-37), a chimeric polynucleotide comprising a polynucleotide that regulates transcription in a cell linked to a polynucleotide encoding a fusion protein comprising a portion of an oleosin obtained from plant and a heterologous protein of interest which is

further linked to a polynucleotide capable of terminating transcription in a plant cell, (pages 2-3). The oleosin used by Moloney et al. comprises at least the central domain (page 16, line 27). The method of Moloney et al. comprises growing said transformed plant host cell under conditions permitting expression of said fusion polypeptide, isolating oil bodies comprising said fusion polypeptide and washing said oil bodies comprised of intact oil bodies via centrifugation (pages 2-3 and 10-11). Centrifugation is given as an example of "washing oil bodies", page 12. Also, since Moloney et al. also teaches that the enzyme of the fusion protein retains its enzymatic properties (page 21) indicating the heterologous protein is intact, Examiner takes the position that the "washed oil body preparation" comprising the fusion protein of Moloney et al. is "substantially intact". Moloney et al. provides several advantages in producing a heterologous protein in plant cells by expressing a fusion protein comprising the protein of interest and an oleosin, such as efficient large scale production of the protein (page 2, lines 1-9).

The difference between the reference of et al. and the instant invention is that the reference of Moloney et al. does not teach a method of emulsifying the washed oil bodies comprising the fusion protein, wherein the heterologous protein is a thioredoxin or a thioredoxin reductase.

Polynucleotides encoding many thioredoxin and thioredoxin reductases are known in the art see NiceZyme: EC 1.8.1.9 – cited previously on form PTO-892). Wieles et al. (cited previously on form PTO-892) discloses a polynucleotide encoding a thioredoxin and thioredoxin reductase and production of thioredoxin and thioredoxin

reductase expressed in bacteria (abstract and pages 921-922). Wieles et al. also discloses that thioredoxin and thioredoxin reductase are involved in redox regulation and catalytic mechanism (abstract and page 921). Wielses et al. does not disclose expression and production of thioredoxin and thioredoxin reductase in plant cells or rapeseed cells.

Deckers et al. (WO 98/53698) – form PTO-1449) discloses a method of preparing an emulsion formulation by (1) obtaining intact oil bodies from various plant cells, (2) washing the intact oil bodies and (3) formulating the washed oil body preparation into an emulsion (page 3, lines 5-38 and page 8, line 20 through page 14, line 30), wherein said emulsion formulations are advantageous in their use in food, cosmetic, pharmaceutical and industrial products (page 3, lines 5-13).

Therefore, combining the teachings of Moloney et al., Wieles et al., and Deckers et al., it would have been obvious to one having ordinary skill in the art to modify the method of Moloney et al. by making a chimeric construct comprising a fusion protein wherein the heterologous protein is the thioredoxin or thioredoxin reductase of Wieles et al., express the chimeric construct in a plant host cell, such as a rapeseed cell, and to formulate the fusion protein into an emulsion using the method of Deckers et al. One of ordinary skill in the art would have been motivated to use thioredoxin or thioredoxin reductase as the heterologous protein in the fusion protein of Moloney et al. in order to inexpensively produce thioredoxin and thioredoxin reductase in plant cells. One of ordinary skill in the art would have been motivated to formulate the fusion protein into an emulsion for use in pharmaceutical products. One of ordinary skill in the art would have

had a reasonable expectation of success of making a fusion protein and isolating the fusion protein since Moloney et al. disclose a method of making a polynucleotide encoding a fusion proteins comprising oleosins and heterologous protein. One of ordinary skill in the art would have had a reasonable expectation of success in making an emulsion comprising said fusion protein since Deckers et al. discloses a method of formulating an emulsion comprising oil bodies.

Therefore, the above references render claims 14-15, 18 and 29-31 *prima facie* obvious to one of ordinary skill in the art.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Yong D. Pak
Primary Patent Examiner 1652